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Impact of prescription drug monitoring programs and pill mill laws on high-risk opioid prescribers: A comparative interrupted time series analysis

Hsien-Yen Chang^{a,b}, Tatyana Lyapustina^c, Lainie Rutkow^a, Matthew Daubresse^{b,c}, Matt Richey^d, Mark Faul^e, Elizabeth A. Stuart^{a,b,f,g}, and G. Caleb Alexander^{b,c,h,*}

- ^a Department of Health Policy and Management, Johns Hopkins Bloomberg School of Public Health, 624 N. Broadway St., Baltimore, MD 21205, United States
- ^b Center for Drug Safety and Effectiveness, Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe St. W6035, Baltimore, MD 21205, United States
- ^c Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe St. W6035, Baltimore, MD 21205, United States
- ^d Department of Mathematics, Statistics, and Computer Science, St. Olaf College, Regents Hall of Science 302, Northfield, MN 55057, United States
- ^e Centers for Disease Control and Prevention, National Center for Injury Prevention and Control, 4770 Buford Hwy, NE Mail Stop MS F-63 Atlanta, GA 30341, United States
- f Department of Mental Health, Johns Hopkins Bloomberg School of Public Health, 624 N. Broadway, 8th Floor, Baltimore, MD 21205, United States

Contributors

HC designed the study, managed data, performed analyses, and drafted the manuscript. TT interpreted results and drafted the manuscript. LR designed the study, revised the manuscript and provided critical comments. MD revised the manuscript and provided critical comments. MF revised the manuscript and provided critical comments. EAS designed the study, provided critical comments and revised the manuscript. GCA designed the study, secured data, and drafted the manuscript. HC, MD and GCA had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. All authors approved of the final manuscript.

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Conflict of interest

Dr. Alexander is Chair of the FDA's Peripheral and Central Nervous System Advisory Committee; serves as a paid consultant to PainNavigator, a mobile startup to improve patients' pain management; serves as a paid consultant to IMS Health; and serves on an IMS Health scientific advisory board. This arrangement has been reviewed and approved by Johns Hopkins University in accordance with its conflict of interest policies. The statements, findings, conclusions, views, and opinions contained and expressed in this article are based in part on data obtained under license from the following IMS Health Incorporated information service(s): IMS Health LifeLink LRx Database[®] (2010–2012), IMS Health Incorporated. All Rights Reserved. The statements, findings, conclusions, views, and opinions contained and expressed herein are not necessarily those of IMS Health Incorporated or any of its affiliated or subsidiary entities.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.drugalcdep. 2016.04.033.

^{*} Corresponding author at: Center for Drug Safety and Effectiveness, Johns Hopkins Bloomberg School of Public Health, 615 N Wolfe St. W6035, Baltimore, MD 21205, United States. galexand@jhsph.edu (G.C. Alexander). hchang24@jhmi.edu (H.-Y. Chang), tlyapus1@jhmi.edu (T. Lyapustina), lrutkow@jhu.edu (L. Rutkow), mdaubre1@jhu.edu (M. Daubresse), richeym@stolaf.edu (M. Richey), mgf7@cdc.gov (M. Faul), estuart@jhsph.edu (E.A. Stuart).

⁹ Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health, 624 N. Broadway, 8th Floor, Baltimore, MD 21205, United States

^h Division of General Internal Medicine, Johns Hopkins Medicine, 615 N Wolfe St., Baltimore, MD 21205, United States

Abstract

Background—Prescription drug monitoring programs (PDMPs) and pill mill laws were implemented to reduce opioid-related injuries/deaths. We evaluated their effects on high-risk prescribers in Florida.

Methods—We used IMS Health's LRx Lifelink database between July 2010 and September 2012 to identify opioid-prescribing prescribers in Florida (intervention state, N: 38,465) and Georgia (control state, N: 18,566). The pre-intervention, intervention, and post-intervention periods were: July 2010–June 2011, July 2011–September 2011, and October 2011–September 2012. High-risk prescribers were those in the top 5th percentile of opioid volume during four consecutive calendar quarters. We applied comparative interrupted time series models to evaluate policy effects on clinical practices and monthly prescribing measures for low-risk/high-risk prescribers.

Results—We identified 1526 (4.0%) high-risk prescribers in Florida, accounting for 67% of total opioid volume and 40% of total opioid prescriptions. Relative to their lower-risk counterparts, they wrote sixteen times more monthly opioid prescriptions (79 vs. 5, p < 0.01), and had more prescription-filling patients receiving opioids (47% vs. 19%, p < 0.01). Following policy implementation, Florida's high-risk providers experienced large relative reductions in opioid patients and opioid prescriptions (–536 patients/month, 95% confidence intervals [CI] –829 to –243; –847 prescriptions/month, CI –1498 to –197), morphine equivalent dose (–0.88 mg/month, CI –1.13 to –0.62), and total opioid volume (–3.88 kg/month, CI –5.14 to –2.62). Low-risk providers did not experience statistically significantly relative reductions, nor did policy implementation affect the status of being high- vs. low- risk prescribers.

Conclusions—High-risk prescribers are disproportionately responsive to state policies. However, opioidsprescribing remains highly concentrated among high-risk providers.

Keywords

High-risk opioid prescribing; Prescription drug abuse; Prescription drug monitoring program; Pill mill law; Time series analysis

1. Introduction

Prescription opioid addiction and non-medical use are significant public health problems, responsible for about 44 daily overdose deaths in the United States (Kolodny et al., 2015; United States Department of Health and Human Services, Centers for Disease Control and Prevention, 2015). From 2000 to 2010, large increases in opioid prescription among ambulatory and emergency visits coincided with reductions in use of non-opioid analgesics and an unchanging prevalence of pain among patients (Chang et al., 2014; Daubresse et al., 2013). The burden of opioid-related morbidity has increased markedly over the past decade, with a 153% increase in the rate of opioid-related emergency department visits between

2004 and 2011 (Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality, 2013). Similarly, the age adjusted death rate attributable to prescription opioids quadrupled between 1999 and 2009, surpassing that of stimulants, heroin, and other prescription drugs (Calcaterra et al., 2013). These problems are not limited to the United States; the United Kingdom and other European countries also face increasing use of opioids for non-cancer pain (Stannard, 2013), high number of individuals estimated to be addicted to prescription drugs (Dhalla et al., 2011b), and an increase in drug-related deaths (Dhalla et al., 2011b; Giraudon et al., 2013).

Although there are no magic bullets to address these issues, policy makers play an important role in shaping regulatory, payment and public health policies to reduce opioid-related injuries and deaths (Dhalla et al., 2011b; Franklin et al., 2015; Giraudon et al., 2013; Lyapustina et al., 2016; Stannard, 2013; Stewart and Basler, 2013). Prescriber-oriented interventions, such as updating the guidelines on opioid prescription, have been adopted in many countries, but their penetration is unknown and following the guidelines is not mandatory (Giraudon et al., 2013). Establishing regulatory monitoring of prescription opioids has also been proposed in the United Kingdom (Stewart and Basler, 2013), and implemented at many states in the United States (Florida Office of the Attorney General, 2015; United States Department of Justice, Drug Enforcement Administration, 2011). For example, state policy-makers in the United States have used prescription drug monitoring programs (PDMPs) and "pill mill" laws to address the prescription opioid epidemic. Although these state-sponsored programs are used for a variety of clinical, regulatory and educational purposes, a primary function of PDMPs is to give physicians, pharmacists and other health care providers access to patients' prescription histories to improve identification and management of individuals at high risk of opioid abuse or diversion (United States Department of Justice and Drug Enforcement Administration, 2011). In contrast, pill mill laws establish state-level regulatory oversight of pain management clinics, including the establishment of prescribing and dispensing requirements, and create penalties for those who do not comply with their requirements (United States Department of Health and Human Services, Centers for Disease Control and Prevention, 2012). While there is growing evidence regarding the effect of these approaches on opioid sales (Haegerich et al., 2014; Rutkow et al., 2015), overdoses (Sauber-Schatz et al., 2013), and deaths (Delcher et al., 2015), less is known about how they affect specific groups of prescribers. This is important, as approximately 20% of U.S. physicians are responsible for prescribing 80% of all opioid analgesics (Blumenschein et al., 2010; Dhalla et al., 2011a; Swedlow et al., 2011).

We previously demonstrated that Florida's PDMP and pill mill law were associated with modest decreases in opioid prescribing concentrated among providers with higher baseline opioid volume (Rutkow et al., 2015). However, in that analysis, which focused on Florida because of disproportionate levels of opioid-related morbidity and mortality in the state, we used a crude measure to characterize high-volume prescribers and limited our analysis to a select number of prescribing outcomes. In the current analysis, we use a rigorous method of identifying several groups of high-risk prescribers and, in addition to more fully characterizing them, we evaluate the effect of Florida's policies on their clinical practices, such as their total number of prescription-filling patients with an opioid prescription.

Furthermore, we characterize the concentration of opioid volume and prescriptions among this group of prescribers as well as how the policies of interest impact these measures.

2. Material and methods

2.1. Data

Using data from IMS Health's LifeLink LRx database, we examined anonymized, individual-level prescription claims, which represented approximately 65% of all retail prescription transactions in the United States. The data are automatically transmitted to IMS Health on a weekly basis from pharmacies in retail and food stores, as well as independent and mass merchandiser pharmacies. Claims data include National Drug Code (NDC)-level product information, quantity dispensed, days supply, payment source (Medicare, Medicaid, commercial insurer, or cash), and the five digit zip code of the dispensing pharmacy. Patient information includes sex, year of birth, and date of first entry into the data set. Prescriber information, derived from the American Medical Association masterfile, includes prescriber specialty and zip code.

2.2. Time segments and cohort derivation

Our analysis was based on a 12-month pre- and post-intervention observation period. The pre-intervention period extended from July 2010 through June 2011. The policy implementation period (i.e., intervention period) included the 3 months between July 2011 through September 2011, representing the time during which Florida's PDMP and relevant aspects of its pill mill law were put into effect. The post-intervention period spanned October 2011 through September 2012.

Approximately 12 million individuals who filled at least one prescription in Florida or Georgia from July 2010 to September 2012 were identified. Among these individuals, we excluded 3.6 million individuals who filled prescriptions from stores that did not consistently report data to IMS Health throughout the study period (no reported data within the first three and last three month of the study period). We also excluded 4.3 million individuals (36%) without any pharmacy claims within three months of the first and last months of the study period. Furthermore, we excluded approximately 2% of transactions with erroneous or extreme values (e.g., negative quantities dispensed or transactions with morphine milligram equivalents (MME) exceeding 360 milligrams [mg] per transaction). In the end, we included 12.02 million eligible opioid prescriptions in the analysis.

From these opioid prescriptions, we identified 57,031 prescribers who had prescribed at least one opioid in Florida or Georgia in the 12-month pre-intervention period. Although we included non-physician prescribers such as dentists and nurse practitioners, we excluded 336 veterinarians. To define high-risk prescribers, we divided the 12-month pre-intervention period into four quarters and calculated each prescriber's total opioid volume, the sum of MME associated with every transaction, during each quarter. In each state, we flagged prescribers who were in the top 5th percentile of opioid volume in each calendar quarter, and we defined high-risk prescribers as those who were flagged for each of the four pre-intervention quarters. Low-risk prescribers were defined as those who did not qualify for the

high-risk category. We also examined two subsets of high-risk prescribers: (1) "high-risk/high-prescription": high-risk prescribers who were also in the top 5th percentile of the *proportion of all prescriptions* dispensed as opioids, across all four quarters during the preintervention period, and (2) "high-risk/high-patient": high-risk prescribers who were also in the top 5th percentile of the *proportion of all prescription-filling patients* receiving opioids, across all four quarters during the pre-intervention period. These four cohorts of prescribers and their respective numbers in Florida were: low-risk (n = 36,939), high-risk (n = 1,526), high-risk/high-prescription (n = 196), and high-risk/high-patient (n = 343).

We selected Georgia as a control state for this analysis due to its close geographic proximity to Florida, its similarity in baseline opioid utilization trends, and its absence of a PDMP or pill mill law during our analysis period.

2.3. Outcomes

We examined seven outcomes, each of which was derived on a monthly basis and summarized by group and state. First, we examined the total number of patients with any opioid prescription, a measure that suggests the extent to which providers are willing to prescribe opioids. Second, we calculated the proportion of prescriptions dispensed as opioids among all prescriptions, an indicator of the relative frequency of opioids among all prescriptions. Third, we derived the proportion of patients with at least one opioid prescription among all patients filling prescriptions, an indicator of the relative use of opioids among patients. Fourth, we quantified the average morphine milligram equilvalent (MME) per transaction, which provides a measure of opioid use within individual transactions. As MME increases, risk of opioid-related morbidity and mortality also increases (Chou et al., 2015). Fifth, we quantified total opioid volume prescribed using morphine equilvalent doses (MED). This measure considers differences in molecules, quantity and strength of doses dispensed, and provides a method of standardizing opioid prescriptions (Gwira Baumblatt et al., 2014; Nuckols et al., 2014). Sixth, we examined average days supply per transaction, since a greater days supply may lead to abuse, diversion and overdose. Seventh, we quantified the total number of opioid prescriptions dispensed, which could vary independently of measures such as total opioid volume or MME per transaction.

We also examined the probability of being a high-risk prescriber in the post-implementation period among four cohorts of prescribers (low-risk prescribers, high-risk prescribers, high-risk/high-patient prescribers), as well as the degree of opioid concentration (total opioid volume and number of opioid prescriptions) within high-risk prescribers prior to and following policy implementation.

2.4. Analysis

We conducted our analysis using a comparative interrupted time series framework. This method allowed us to correct for autocorrelation across time while determining the effect of Florida's laws on our outcomes of interest (Johnson et al., 2014). We derived our outcomes on a monthly basis but collated the three months required for policy implantation into one observation, resulting in 25 observations per state. These observations provided a

comparative change of monthly levels and trends in the outcomes between Florida and Georgia before and after Florida's policy changes.

We applied linear regression to the data, including two interaction terms: an interaction of the state indicator (FL or GA) and a period indicator (pre or post), representing the effect of the policies on the level of the outcome; and an interaction of the state indicator and a post-intervention month indicator, representing the effect of the policies on the rate of change (trend). We adjusted for autocorrelation across time using the generalized Durbin-Watson test and included appropriate autocorrelation orders in our regression models. We ran one model separately for each cohort of prescribers.

We performed two main sensitivity analyses. First, we varied the length of observation for evaluating policy impact to 18 months and 6 months. Second, we varied the threshold to define high-risk prescribers (e.g., top 1%, 3%, 5%, etc. of total opioid volume in each of four consecutive pre-policy calendar quarters) and evaluated if changes in opioid concentration and high-risk status following policy implementation showed similar patterns across all thresholds.

The R² of all models was higher than 0.80, reflecting large sample sizes and relatively little variation in the outcomes of interest over time. All analyses were completed using SAS version 9.4 (proc autoreg command with nlag function).

3. Results

3.1. Characteristics of high-risk prescribers

A total of 1,526 of 38,465 Florida prescribers (3.97%) were identified as high-risk; these prescribers accounted for 66.59% of the opioid volume and 39.99% of the total opioid prescriptions dispensed in Florida during the pre-intervention period. Prescribers with high opioid volumes during any one quarter had a high likelihood of having high opioid volumes during other three calendar quarters (Spearman correlation coefficient: 0.79–0.87). Nearly identical patterns were observed in Georgia, both with respect to the proportion of prescribers identified as high risk and the correlation between prescriber opioid volumes over time.

Table 1 provides characteristics of each risk cohort in Florida. High-risk prescribers wrote about five times the number of prescriptions (465 vs. 82 total monthly prescriptions) and sixteen times the number of opioid prescriptions (79 vs. 5 monthly opioid prescriptions) relative to their lower-risk counterparts. High-risk prescribers were more likely to be primary care physicians (54% vs. 25%), to have patients filling opioid prescriptions (47% vs. 19%), to have patients using Medicare Part D (29% vs. 16%) and to have cash-paying patients (7% vs. 4%). All these comparisons between low-risk and high-risk prescribers were statistically significant at p = 0.05 level.

High-risk/high-prescription and high-risk/high-patient subsets wrote fewer total prescriptions than other high-risk prescribers, but approximately 50% greater opioid prescriptions. These individuals tended to be Surgery, Anesthesia or Pain subspecialists, and

the proportion of their prescription-filling patients with an opioid prescription was over 80%, compared with 47% among all high-risk prescribers and 19% among low-risk prescribers.

3.2. Effect of policy changes stratified by prescriber risk

Table 2 reveals the impact of Florida's PDMP and pill mill law on prescribers by their baseline level of risk, as compared to Georgia. Across all four groups and seven outcomes, comparative changes in levels were not statistically significant. By contrast, there were clinically significantly relative reductions in monthly trends in many of the outcomes of interest among high-risk prescribers. For example, there was a monthly relative decline in number of patients with an opioid prescription of 536 patients/month (95% confidence interval [CI] –829 to –243), average morphine equivalent dose per transaction of –0.88 mg/month/transaction (95% CI –1.13 to –0.62), a relative reduction in monthly total opioid volume of –3.88 kg/month (95% CI –5.14 to –2.62), and a relative decrease in number of opioid prescriptions of 847 prescription/month (95% CI – 1498 to –197). In contrast, there was a slight relative increase in average days' supply of 0.02 days/month/transaction (95% CI 0.00–0.04). Among the low-risk prescribers, there were no statistically significant effects on the level or trend across all outcomes examined.

We observed fewer statistically significant policy effects among the high-risk/high-patient and high-risk/high-prescription prescribers, although both groups did experience statistically significantly relative reductions in monthly average morphine milligram equivalent (MME) and total opioid volume, with larger relative reductions among high-risk/high-patient prescribers (-0.84 [95% CIs -1.04, -0.64] vs. -0.27 [95% CIs -0.42,-0.11] mg/month/ transaction for morphine equivalent dose; -1.92 [95% CIs -2.66,-1.19] vs. -0.41 [95% CIs -0.70,-0.12] kg/month for total opioid volume).

Sensitivity analysis indicated similar results with varying lengths of observation (Appendices 1 and 2).

3.3. Observed versus predicted outcomes

Table 3 and the Fig. 1 show the difference between the observed outcomes and the predicted outcomes had Florida's PDMP and pill mill law not been implemented. Across all four groups, there was a greater difference between the observed and predicted outcomes during the second 6 months after the policy changes than during the first 6 months. For example, during the second 6 months, the observed MME was 13.7% and 4.9% less than the predicted values among high- and low-risk prescribers, respectively. However, these differences were only 5.7% and 0.1% less than predicted values during the first six months after the policy change. The largest difference in the impact of the policies between high-risk and low-risk prescribers was on total opioid volume (estimated policy effect at one year of a reduction of 13.5% vs. an increase 11.1%) and morphine-equivalent dose (reduction of 9.6% vs. 1.2%), with smaller differences on outcomes such as number of opioid prescriptions and number of patients filling prescriptions who received an opioid. Between the two high-risk subgroups, there were larger impacts for the high-risk/high-patient group than the high-risk/high-prescription group; for example, the policies were associated with 14.2% and 6.0% reductions in total opioid volume, respectively. Both high-risk subgroups had a small

increase in actual percentages of opioid prescription and patients with any opioid prescription relative to the predicted situation without the policy change.

3.4. Changes in opioid concentration and high-risk status following policy

The 4% of Florida prescribers who were characterized as high-risk accounted for a similar proportion of all opioids after the policy as before the policies were implemented (pre-policy opioid volume 66.59%, post-policy opioid volume 67.30%; pre-policy proportion of all opioid prescriptions 39.99%, post-policy proportion of all opioid prescriptions 41.36%). In other words, most prescribers – 99% of low-risk prescribers and 83% of high-risk prescribers – maintained their opioid-prescribing status from the pre- to post-implementation period.

Sensitivity analysis showed that the same patterns were observed across all thresholds to define being high-risk prescribers (Supplementary Material 3).

4. Discussion

We quantified the effect of Florida's PDMP and pill mill law on several populations of highrisk prescribers. The 4% of prescribers who we deemed high-risk accounted for two-thirds of the opioid volume and two-fifths of the total opioid prescriptions dispensed in Florida during the pre-intervention period. Florida's PDMP and pill mill law were associated with statistically and clinically significantly relative reductions in four of the seven outcomes that we examined among high-risk prescribers, with virtually no effect on their lower-risk counterparts. Despite this, even following policy implementation, prescribing remained highly concentrated among these same high-risk providers.

These results are important in light of the magnitude of injuries and deaths associated with opioid use, as well as the interest policy-makers and other stakeholders have in interventions such as PDMPs and pill mill laws to address these outcomes. The effect of such policies is of particular interest in states such as Florida, which experienced one of the most rapid increases in opioid-related morbidity and mortality during the decade prior to policy implementation (Florida Office of the Attorney General, 2015). During that time, Florida also epitomized the extreme differences in the extent to which providers prescribe opioids: in 2010, 98 of the 100 highest opioid prescribers in the nation were practicing in Florida (Johnson et al., 2014). Here, we extend prior work by rigorously identifying and characterizing subgroups of high-risk prescribers as well as quantifying the effect of the policy changes of interest on outcomes such as the composition of their patient panels.

Our finding that high-risk opioid prescribers are disproportionately responsive to state policies allows for policy-makers to understand the population of prescribers whose behavior is most likely to be affected by state policies such as PDMPs and Pill Mill laws. Not all prescribers are affected equally. To the degree that these policies are intended to target the outlying prescribers, they appear to be working. Nonetheless, important questions remain regarding many dimensions of these programs, but that reductions are concentrated in the highest volume prescribers is of interest. Another finding regarding the high concentration of opioid prescribing on the same prescribers even following policy

implementation suggests the suitability and importance of other regulatory, payment or enforcement interventions that target small subsets of prescribers.

In addition to the evaluation of the overall policy impact, many studies have focused on patient-level predictors of opioid abuse and diversion (Gwira Baumblatt et al., 2014; Paulozzi et al., 2012). Furthermore, prescribing guidelines have been increasingly scrutinized and reevaluated (Nuckols et al., 2014). Despite this, data on provider-level factors predicting inappropriate prescribing have been more limited. Our findings highlight that a small subset of high-risk prescribers are responsible for prescribing a vastly disproportionate fraction of the opioids in circulation today (Chou et al., 2015); although policies may decrease the overall volume of opioids on the market, they do not alter this heavily concentrated pattern.

Surprisingly, we found fewer effects among subpopulations of prescribers who were defined not only by high opioid volume at baseline, but also by a high proportion of patients or prescriptions accounted for by opioids. Our sample sizes in these subgroups were much smaller and thus we may have had insufficient statistical power to discern changes that took place. In addition, these prescribers may have had a greater tendency to be writing clinically appropriate prescriptions (e.g., different patient case-mix) and thus they may have been less vulnerable to the effects of the policies examined.

Since Florida implemented its PDMP and pill mill law around the same time, we are not able to statistically disentangle the effects of these two policies. The implementation of Florida's pill mill law allowed law enforcement agents to raid clinics, seize assets, and make arrests, resulting in the closure of approximately 250 pill mills in the state by 2013 and reducing the state's share of the nation's top oxycodone prescribers from 98 in 2010–0 in 2013 (Johnson et al., 2014). By contrast, the PDMP has allowed for providers to access patients' prescribing histories at the point of care, and for enforcement to use PDMP data for active investigations. Although the policies were designed with different goals in mind, both policies likely contributed to the changes we observed.

Our study has a number of limitations. First, our analysis was limited to retail prescription claims which, while capturing the majority of opioid transactions, nonetheless excludes sales from direct physician dispensing – which was forbidden by the pill mill law starting in July 2011 – as well those occurring in settings such as hospitals, nursing homes, and other institutions. The absence of data capturing physician dispensing may lead us to underestimate the effect of Florida's policies. Second, our data source prevented us from assessing whether transactions were clinically indicated or were associated with opioid-related morbidity or mortality. Our methods of identifying high-risk prescribers are imprecise and intended for screening purposes and are not intended to indicate the legality or quality of any individual providers' prescribing behavior. Despite this, our methods have face and construct validity and, given the ubiquity of automated data and the magnitude of the epidemic, these approaches will remain important in the coming decade (Cepeda et al., 2012; Paulozzi et al., 2014). Third, while our derivation of a closed cohort of stores and patients reduced the bias introduced from an open cohort, it limited the number of observations available for analysis. Finally, we were unable to identify the independent

effects of Florida's PDMP and pill mill laws given that they were enacted within a few months of each another.

High-risk opioid prescribers are a unique group of providers who consistently prescribe higher opioid volumes than their peers and are responsible for having prescribed a disproportionate fraction of the opioids in circulation today. We found that the prescribing behavior of the small subset of Florida prescribers who were high-risk was significantly affected by Florida's PDMP and pill mill law, while low-risk providers were not similarly impacted. Despite this, even following policy implementation, opioid prescribing remained highly concentrated, suggesting continued opportunities to strategically target initiatives to reduce opioid use and, ultimately, opioid-related morbidity and mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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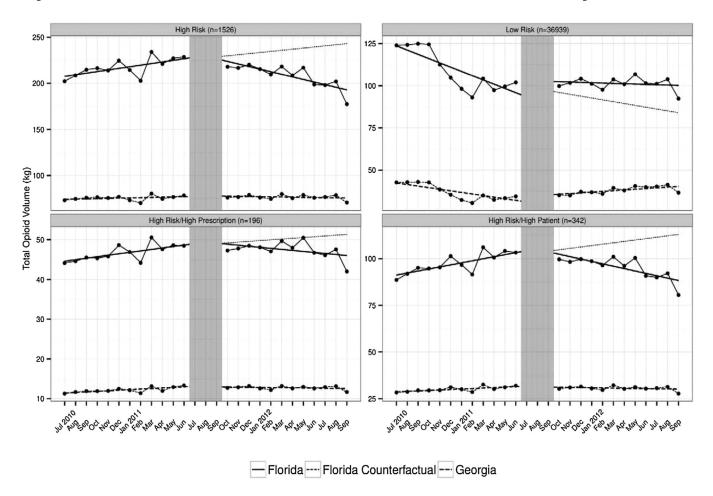


Fig. 1.Effect of Florida's Prescription Drug Monitoring Program and Pill-Mill Law on Opioid Prescribing Volume Among Prescribers Stratified by Baseline Risk.

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	Low-Risk Prescribers N = 36,939	High-Risk Prescribers N = 1526	Subset of High-Risk I	Prescribers
			High-Prescription N = 196	High-Patient N = 343
Provider characteristics b				
Average monthly prescriptions, N	82.23	464.78	195.76	226.71
Average monthly opioid prescriptions, N	4.92	79.34	119.29	120.85
Provider Specialty, %				
Dentist	18.21	0	0	0
Emergency Medicine	4.24	1.31	0.51	0.87
NMD	4.13	0	0	0
Other	25.65	14.68	15.31	22.45
Primary Care	25.4	54.26	8.67	12.54
Psychiatry/Neurology	3.96	5.5	0	2.62
Surgery/Anesthesia/Pain	18.42	24.25	75.51	61.52
Patient characteristics ^b				
Monthly patients with any prescription, N	37.26	164.97	100.41	101.12
Monthly patients with opioid prescription, N	4.17	59.57	84.02	84.38
Monthly prescriptions per patient, N	1.72	2.68	1.98	2.29
Monthly opioid prescriptions per patient, N	0.75	1.35	1.48	1.48
Proportion of opioids among all prescriptions, %	13.01	27.7	62.23	55.63
Proportion of patients with an opioid prescription, %	18.68	46.77	83.09	83.37
Payment characteristics for opioid prescriptions b				
Monthly patients with an opioid cash payment, N	0.27	3.94	4.14	5.41
Monthly opioids paid in cash, %	4.26	7.06	5.62	7.7
Monthly opioids paid through Medicaid, %	3.75	5	2.28	3.8
Monthly opioids paid through Medicare Part D, %	15.52	28.62	26.57	25.05
Monthly opioids paid through Commercial Insurer, $\%$	41.62	59.29	65.53	63.45
Prescribing risk status after policy change b				
Low-Risk Prescribers, %	99.13	16.91	6.12	10.79
High-Risk Prescribers, %	0.82	83.09	93.88	89.21

Source: IMS Health Lifelink LRx Data, 2010–2012.

^aHigh-risk prescribers were those who in four consecutive quarters were in the 95th percentile or higher regarding total opioid volume; "high prescription" based on individuals who also were also in 95th percentile or higher on fraction of all prescriptions dispensed as opioids; "high patient" based on prescribers who were in 95th percentile or higher on fraction of all prescription filling patients receiving opioids.

 Table 2

 Impact of florida's pdmp and pill mill law on monthly outcomes among high-risk and low-risk prescribers.

	Low-Risk Prescribers	High-Risk Prescribers N	Subset of High-Risk Pres	scribers
	N = 36,939	= 1526	High-Prescription N = 196	High-Patient N = 343
Comparative Change in Levels				
Opioid Patients, N	-4211 (-10932,2510)	-524 (-2799,1752)	-89 (-794,616)	71 (-1233,1375)
Opioid Prescriptions, % of all prescriptions	-0.27 (-1.07,0.53)	0.25 (-0.54,1.04)	0.67 (-0.61,1.94)	0.37 (-0.57,1.30)
Opioid Patients, % of all patients	-0.05 (-0.48,0.37)	0.09 (-0.43,0.60)	0.42 (-0.39,1.24)	0.41 (-0.34,1.16)
Morphine Equivalent Dose, mg	0.26 (-3.31,3.83)	-0.07 (-1.59,1.44)	-1.01 (-2.10,0.09)	-0.54 (-1.87,0.78)
Total Opioid Volume, kg	3.51 (-7.02,14.02)	1.56 (-8.13,11.25)	0.34 (-2.03,2.71)	1 (-4.46,6.47)
Days' Supply	0.01 (-0.04,0.03)	0.13 (-0.01,0.26)	0.08 (-0.11,0.28)	0.03 (-0.10,0.15)
Opioid Prescriptions, N	-4322 (-13036,4392)	-996 (-5782,3791)	2 (-1068,1071)	471 (-1824,2766)
Comparative Change in Monthly Trends				
Opioid Patients, N	399 (-461,1259)	-536***(-829,-243)	-37 (-137,63)	-194*(-351,-6)
Opioid Prescriptions, % of all prescriptions	-0.06 (-0.19,0.07)	-0.08 (-0.20,-0.03)	0.07 (-0.12,0.25)	-0.03 (-0.17,0.10)
Opioid Patients, % of all patients	-0.04 (-0.11,0.04)	-0.08 (-0.16,0.00)	0.05 (-0.07,0.17)	0.07 (-0.04,0.18)
Morphine Equivalent Dose, mg	-0.14 (-0.78,0.51)	-0.88**(-1.13,-0.62)	-0.27***(-0.42,-0.11)	-0.84 ** (-1.04,-0.64)
Total Opioid Volume, kg	0.93 (-0.65,2.51)	-3.88** (-5.14,-2.62)	-0.41**(-0.70,-0.12)	-1.92 ** (-2.66,-1.19)
Days' Supply	-0.04 (-0.10,0.02)	0.02*(0.00,0.04)	0.02 (0.00,0.05)	-0.01 (-0.02,0.01)
Opioid Prescriptions, N	482 (-630,1594)	-847*(-1498,-197)	-30 (-160,101)	-279 (-588,30)

Source: IMS Health Lifelink LRx Data, 2010–2012.

^{*} P<0.05

^{**} P<0.01.

Table 3

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Difference between monthly actual and predicted outcomes without policy implementation.

	First Hal	First Half-Year After Policy		Second I	Second Half-Year After Policy		Cumulat	Cumulative One Year After Policy	licv
	Actual	Predicted w/o Law	Difference, %	Actual	Predicted w/o Law	Difference, %	Actual	Predicted w/o Law	Difference, %
Low-Risk Prescribers ($N = 36,939$)									
Opioid Patients, N	143473	147141	2.56%	146962	146526	-0.30%	145217	146834	1.11%
Opioid Prescriptions, % of all rx	5.65	5.91	4.60%	5.93	6.24	5.23%	5.79	6.07	4.84%
Opioid Patients, % of all patients	10.52	11.13	5.80%	11	11.7	6.36%	10.76	11.42	6.13%
Morphine Equivalent Dose, mg	40.15	40.18	0.07%	40.03	41.99	4.90%	40.09	40.58	1.22%
Total Opioid Volume, kg	101.37	93.26	-8.00%	101.08	86.78	-14.15%	101.23	90.02	-11.07%
Days' Supply	15.42	15.49	0.45%	15.67	15.77	0.64%	15.34	15.58	1.56%
Opioid Prescriptions, N	168837	172439	2.13%	172455	171316	~99.0-	170646	171878	0.72%
High-Risk Prescribers (N= 1526)									
Opioid Patients, N	91643	94707	3.34%	90374	20996	%06.9	91008	95657	5.11%
Opioid Prescriptions, % of all rx	17.4	17.74	1.95%	17.65	18.3	3.68%	17.53	18.02	2.80%
Opioid Patients, % of all patients	36.47	36.72	0.69%	36.62	37.11	1.34%	36.54	36.92	1.04%
Morphine Equivalent Dose, mg	70.08	74.06	5.68%	96.99	76.14	13.71%	68.52	75.1	%09.6
Total Opioid Volume, kg	216.44	232.9	7.60%	200.33	240.11	19.86%	208.39	236.5	13.49%
Days' Supply	25.53	25.29	-0.94%	25.46	25.12	-1.34%	25.49	25.2	-1.14%
Opioid Prescriptions, N	121583	126515	4.06%	119131	129181	8.44%	120357	127848	6.22%
High-Risk High-Prescription ($N = 196$)									
Opioid Patients, N	17414	17668	1.46%	17913	18314	2.24%	17664	17991	1.85%
Opioid Prescriptions, % of all rx	60.92	60.31	-1.00%	61.07	60.07	-1.64%	60.09	60.19	-1.31%
Opioid Patients, % of all patients	83.63	82.74	-1.06%	83.57	82.17	-1.68%	83.6	82.46	-1.36%
Morphine Equivalent Dose, mg	74.96	77.17	2.95%	71.94	75.73	5.27%	73.45	76.45	4.08%
Total Opioid Volume, kg	48.07	49.69	3.37%	46.82	50.84	8.59%	47.44	50.27	5.97%
Days' Supply	26.23	26.05	~69.0-	26.25	25.94	-1.18%	26.24	25.99	-0.95%
Opioid Prescriptions, N	24487	24666	0.73%	24934	25300	1.47%	24710	24983	1.10%
High-Risk High-Patient (N=343)									
Opioid Patients, N	30470	31220	2.46%	30698	32529	2.96%	30584	31875	4.22%
Opioid Prescriptions, % of all rx	54.09	53.28	-1.50%	54.59	53.45	-2.09%	54.34	53.36	-1.80%

	First Ha	First Half-Year After Policy		Second F	Second Half-Year After Policy		Cumulat	Cumulative One Year After Policy	olicy
	Actual	Predicted w/o Law	Difference, %	Actual	Difference, % Actual Predicted w/o Law	Difference, %	Actual	Difference, % Actual Predicted w/o Law Difference, %	Difference, %
Opioid Patients, % of all patients	83.4	83.21	-0.23%	83.03	82.93	-0.12%	83.22	82.07	-1.38%
Morphine Equivalent Dose, mg	85.41	89.76	5.09%	80.21	89.49	11.57%	82.81	89.62	8.22%
Total Opioid Volume, kg	98.94	106.62	7.76%	91.68	111.08	21.16%	95.31	108.85	14.21%
Days' Supply	26.95	26.95	0.00%	26.9	26.94	0.15%	26.93	26.95	0.07%
Opioid Prescriptions, N	43450	44230	1.80%	43167	45676	5.81%	43309	44953	3.80%

Source: IMS Health Lifelink LRx Data, 2010–2012.

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